NMCP COVID-19 Literature Report #22: Tuesday, 16 June 2020

Prepared By: Tracy Shields, MSIS, AHIP <tracy.c.shields2.civ@mail.mil>
Reference Medical Librarian; Naval Medical Center Portsmouth, Library Services

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily. Best practice and evidence are constantly shifting during this international public health crisis.

Reports are biweekly, planned for Tuesdays and Fridays.

Statistics

Global 8,065,966 confirmed cases and 437,604 deaths in 188 countries/regions

*United States** top 5 states by cases (Virginia is ranked 12th)

	TOTAL US	NY	NJ	CA	IL	MA
Confirmed Cases	2,115,079	383,944	167,103	155,733	133,016	105,690
Tested	23,984,592	2,991,210	1,116,083	2,868,182	1,210,473	717,231
Recovered	NA	68,851	28,819	NA	NA	NA
Deaths	116,191	30,856	12,708	5,116	6,326	7,647

*see census.gov for current US Population data; NA: not all data available JHU CSSE as of 1100 EDT 16 June 2020

Navy (Department of Defense)

	TOTAL	MIL	CIV	DEP	CTR
Cases	516	324	91	44	57
Hospitalized	8	2	2	1	3
Recovered	3,110	2,431	379	169	131
Deaths	12	1	8	0	3
Cumulative*	3,638	2,756	478	213	191

*cumulative total = active + recovered + deaths DOD dated 15 June 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	55,331	678	246	390	681	387	347	909
Hospitalized	5,643	102	37	43	84	59	53	110
Deaths	1,570	16	5	10	7	12	34	27

VA DOH as of 1100 EDT 16 June 2020

Late Breaking News

The UK-based RECOVERY (Randomised [sic] Evaluation of COVid-19 thERapY) trial aims to identify treatments that may be beneficial for people hospitalized with suspected or confirmed COVID-19. Over 11,500 patients have been randomized to the following treatment arms, or no additional treatment:

- Lopinavir-Ritonavir (commonly used to treat HIV)
- Low-dose Dexamethasone - RECRUITMENT CLOSED TO ADULTS
- Hydroxychloroquine - RECRUITMENT CLOSED
- Azithromycin (a commonly used antibiotic)
- Tocilizumab (an anti-inflammatory treatment given by injection)
- Convalescent plasma (collected from donors who have recovered from COVID-19 and contains antibodies against the SARS-CoV-2 virus)

In a statement released Tuesday, 16 June 2020, the research team reports data from the dexamethasone arm (RECOVERY). They note:

> "On 8 June, recruitment to the dexamethasone arm was halted since, in the view of the trial Steering Committee, sufficient patients had been enrolled to establish whether or not the drug had a meaningful benefit.
>
> A total of 2104 patients were randomised to receive dexamethasone 6 mg once per day (either by mouth or by intravenous injection) for ten days and were compared with 4321 patients randomised to usual care alone. Among the patients who received usual care alone, 28-day mortality was highest in those who required ventilation (41%), intermediate in those patients who required oxygen only (25%), and lowest among those who did not require any respiratory intervention (13%).
>
> Dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88]; p=0.0003) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; p=0.0021). There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75]; p=0.14).
>
> Based on these results, 1 death would be prevented by treatment of around 8 ventilated patients or around 25 patients requiring oxygen alone.
>
> Given the public health importance of these results, we are now working to publish the full details as soon as possible."

For more information about the study, including the protocol and data from the hydroxychloroquine arm, see: https://www.recoverytrial.net/

Selected Primary Literature

Recent—published in peer-reviewed journals within the last 7 days of report's date

Nat Med: Age-dependent effects in the transmission and control of COVID-19 epidemics (16 June 2020)

> "The COVID-19 pandemic has shown a markedly low proportion of cases among children. Age disparities in observed cases could be explained by children having lower susceptibility to infection, lower propensity to show clinical symptoms or both. We evaluate these possibilities by fitting an age-structured mathematical model to epidemic data from China, Italy, Japan, Singapore, Canada and South Korea. We estimate that susceptibility to infection in individuals under 20 years of age is approximately half that of adults aged over 20 years, and that clinical symptoms manifest in 21% (95% credible interval: 12–31%) of infections in 10- to 19-year-olds, rising to 69% (57–82%) of infections in people aged over 70 years. Accordingly, we find that interventions aimed at children might have a relatively small impact on reducing SARS-CoV-2 transmission, particularly if the transmissibility of subclinical infections is low. Our age-specific clinical fraction and susceptibility estimates have implications for the expected global burden of COVID-19, as a result of demographic differences across settings. In countries with younger population structures—such as many low-income countries—the expected per capita incidence of clinical cases would be lower than in countries with older population structures, although it is likely that comorbidities in low-income countries will also influence disease severity. Without effective control measures, regions with relatively older populations could see disproportionally more cases of COVID-19, particularly in the later stages of an unmitigated epidemic."

JAMA: Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium (15 June 2020)

> "In this hospital-wide screening study for SARS-CoV-2 antibodies among hospital staff, neither being directly involved in clinical care nor working in a COVID-19 unit increased the odds of being seropositive, while having a suspected COVID-19 household contact did. The high availability of PPE, high standards of infection prevention, and polymerase chain reaction screening in symptomatic staff, coupled with contact tracing and quarantine, might explain a relatively low seroprevalence….
>
> Quick screening of large cohorts is important to control the pandemic.4 Hospital-wide antibody screening for SARS-CoV-2 can help monitor transmission dynamics and evaluate infection control policies."

JAMA Netw Open: Effects of Sterilization With Hydrogen Peroxide and Chlorine Dioxide on the Filtration Efficiency of N95, KN95, and Surgical Face Masks (15 June 2020)

> "This quality improvement study found that the sterilization processes had different effects on the filtration efficiencies of different masks. Sterilization with H2O2 had fewer negative

effects than ClO2. In addition to considering the overall filtration efficiency, the filtration efficiency for particles similar to infectious agents should be considered. This study has some limitations, including the small variety of mask manufacturers, small sample sizes for each mask and condition, and only 2 sterilization techniques evaluated. In addition, this study only compared the filtration efficiency after 1 sterilization cycle; however, filter material may degrade further after multiple cycles, which should also be investigated. To better protect health care personnel in hospitals, we recommend measuring the respirator's filtration efficiency by aerosol size instead of only measuring the overall filtration efficiency."

MMWR: Coronavirus Disease 2019 Case Surveillance — United States, January 22–May 30, 2020 (15 June 2020)

"As of May 30, 2020, among COVID-19 cases, the most common underlying health conditions were cardiovascular disease (32%), diabetes (30%), and chronic lung disease (18%). Hospitalizations were six times higher and deaths 12 times higher among those with reported underlying conditions compared with those with none reported.

Surveillance at all levels of government, and its continued modernization, is critical for monitoring COVID-19 trends and identifying groups at risk for infection and severe outcomes. These findings highlight the continued need for community mitigation strategies, especially for vulnerable populations, to slow COVID-19 transmission."

J Antibiot: Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen (12 June 2020)

"Ivermectin proposes many potentials effects to treat a range of diseases, with its antimicrobial, antiviral, and anti-cancer properties as a wonder drug. It is highly effective against many microorganisms including some viruses. In this comprehensive systematic review, antiviral effects of ivermectin are summarized including in vitro and in vivo studies over the past 50 years. Several studies reported antiviral effects of ivermectin on RNA viruses such as Zika, dengue, yellow fever, West Nile, Hendra, Newcastle, Venezuelan equine encephalitis, chikungunya, Semliki Forest, Sindbis, Avian influenza A, Porcine Reproductive and Respiratory Syndrome, Human immunodeficiency virus type 1, and severe acute respiratory syndrome coronavirus 2. Furthermore, there are some studies showing antiviral effects of ivermectin against DNA viruses such as Equine herpes type 1, BK polyomavirus, pseudorabies, porcine circovirus 2, and bovine herpesvirus 1. Ivermectin plays a role in several biological mechanisms, therefore it could serve as a potential candidate in the treatment of a wide range of viruses including COVID-19 as well as other types of positive-sense single-stranded RNA viruses. In vivo studies of animal models revealed a broad range of antiviral effects of ivermectin, however, clinical trials are necessary to appraise the potential efficacy of ivermectin in clinical setting."

NEJM: Natural History of Asymptomatic SARS-CoV-2 Infection (12 June 2020)

> This letter to the editor reports on the natural history of asymptomatic infection with SARS-CoV-2 in a cohort from the cruise ship Diamond Princess.
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> "In this cohort, the majority of asymptomatically infected persons remained asymptomatic throughout the course of the infection. The time to the resolution of infection increased with increasing age."

Int J Infect Dis: Comparison of Hospitalized Patients with pneumonia caused by COVID-19 and influenza A in children under 5 years (11 June 2020)

> "This was a retrospective study. Two group of COVID-19 patients (n=57) and influenza A patients (n=59) were enrolled. We analyzed and compared their clinical manifestations, imaging characteristics and treatments.
>
> The proportions of cough (70.2%), fever (54.4%) and gastrointestinal symptoms (14.1%) in COVID-19 patients were lower than those of influenza A patients (98.3%, P <0.001; 84.7%, P <0.001; and 35.6%, P = 0.007; respectively). In addition, COVID-19 patients showed significantly lower levels of leukocytes (7.87 vs. 9.89 ×109/L, P = 0.027), neutrophils (2.43 vs. 5.16 ×109/L, P < 0.001), C-reactive protein (CRP; 3.7 vs. 15.1 mg/L, P = 0.001) and procalcitonin (PCT; 0.09 vs. 0.68 mm/h, P < 0.001), while lymphocyte levels (4.58 vs. 3.56 ×109/L; P = 0.006) were significantly higher compared with influenza A patients. In terms of CT imaging, ground-glass opacification in chest CT was more common in COVID-19 patients than in influenza A patients (42.1% vs. 15%, P = 0.032). In contrast, consolidation was more common in influenza A patients (25%) than that in COVID-19 patients (5.2%, P =0.025).
>
> The clinical manifestations and laboratory tests of COVID-19 children are milder than those of influenza A children under 5 years. Additionally, imaging results more commonly presented as ground-glass opacities in COVID-19 patients."

PNAS: Identifying airborne transmission as the dominant route for the spread of COVID-19 (11 June 2020)

> "We have elucidated the transmission pathways of coronavirus disease 2019 (COVID-19) by analyzing the trend and mitigation measures in the three epicenters. Our results show that the airborne transmission route is highly virulent and dominant for the spread of COVID-19. The mitigation measures are discernable from the trends of the pandemic. Our analysis reveals that the difference with and without mandated face covering represents the determinant in shaping the trends of the pandemic. This protective measure significantly reduces the number of infections. Other mitigation measures, such as social distancing implemented in the United States, are insufficient by themselves in protecting the public. Our work also highlights the necessity that sound science is essential in decision-making for the current and future public health pandemics."

Emerg Infect Dis: Clusters of Coronavirus Disease in Communities, Japan, January–April 2020 (10 June 2020)

> "By investigating the epidemiologic links among cases, we identified 61 COVID-19 clusters in various communities. We observed clusters of COVID-19 cases from 18 (30%) healthcare facilities; 10 (16%) care facilities of other types, such as nursing homes and day care centers; 10 (16%) restaurants or bars; 8 (13%) workplaces; 7 (11%) music-related events, such as live music concerts, chorus group rehearsals, and karaoke parties; 5 (8%) gymnasiums; 2 (3%) ceremonial functions; and 1 (2%) transportation-related incident in an airplane. Most (39/61; 64%) clusters involved 5–10 cases (Figure 1, panel B). The largest cluster involved >100 cases in a hospital, including nosocomial infections and staff infections. The largest non–healthcare-related cluster we observed was among >30 persons who attended a live music concert, including performers, audience members, and event staff. Healthcare and care facilities accounted for >50% of clusters at epidemiologic weeks 11 and 14."

Proc R Soc Lond A Math Phys Sci: A modelling framework to assess the likely effectiveness of facemasks in combination with 'lock-down' in managing the COVID-19 pandemic (10 June 2020)

> "COVID-19 is characterized by an infectious pre-symptomatic period, when newly infected individuals can unwittingly infect others. We are interested in what benefits facemasks could offer as a non-pharmaceutical intervention, especially in the settings where high-technology interventions, such as contact tracing using mobile apps or rapid case detection via molecular tests, are not sustainable. Here, we report the results of two mathematical models and show that facemask use by the public could make a major contribution to reducing the impact of the COVID-19 pandemic. Our intention is to provide a simple modelling framework to examine the dynamics of COVID-19 epidemics when facemasks are worn by the public, with or without imposed ‘lock-down’ periods. Our results are illustrated for a number of plausible values for parameter ranges describing epidemiological processes and mechanistic properties of facemasks, in the absence of current measurements for these values. We show that, when facemasks are used by the public all the time (not just from when symptoms first appear), the effective reproduction number, Re, can be decreased below 1, leading to the mitigation of epidemic spread. Under certain conditions, when lock-down periods are implemented in combination with 100% facemask use, there is vastly less disease spread, secondary and tertiary waves are flattened and the epidemic is brought under control. The effect occurs even when it is assumed that facemasks are only 50% effective at capturing exhaled virus inoculum with an equal or lower efficiency on inhalation. Facemask use by the public has been suggested to be ineffective because wearers may touch their faces more often, thus increasing the probability of contracting COVID-19. For completeness, our models show that facemask adoption provides population-level benefits, even in circumstances where wearers are placed at increased risk. At the time of writing, facemask use by the public has not been recommended in many countries, but a recommendation for wearing face-coverings has just been announced for

Scotland. Even if facemask use began after the start of the first lock-down period, our results show that benefits could still accrue by reducing the risk of the occurrence of further COVID-19 waves. We examine the effects of different rates of facemask adoption without lock-down periods and show that, even at lower levels of adoption, benefits accrue to the facemask wearers. These analyses may explain why some countries, where adoption of facemask use by the public is around 100%, have experienced significantly lower rates of COVID-19 spread and associated deaths. We conclude that facemask use by the public, when used in combination with physical distancing or periods of lock-down, may provide an acceptable way of managing the COVID-19 pandemic and re-opening economic activity. These results are relevant to the developed as well as the developing world, where large numbers of people are resource poor, but fabrication of home-made, effective facemasks is possible. A key message from our analyses to aid the widespread adoption of facemasks would be: 'my mask protects you, your mask protects me'."

ICYMI—recent literature published earlier than 7 days ago, not previously covered

Mayo Clin Proc: Advancing Physician Well-Being: A Population Health Framework (01 June 2020)

"We envision a future state for the profession of medicine characterized by highly engaged, professionally fulfilled, and dedicated physicians practicing in a thoughtfully designed environment. A population health approach to achieve this future state is characterized by an integrated set of universal strategies to promote well-being for all physicians, selective prevention for groups of physicians at higher than average risk, indicated intervention for individual physicians experiencing job-related distress, and unfettered access to treatment for physicians with anxiety, depression, or suicidal ideation. For optimum efficacy, this approach must engage organizations and incite change in the culture of medicine by promulgating a professional environment of self-care, community, peer-support, and help-seeking when distress occurs."

Preprints—not yet peer-reviewed papers

*bioRxiv and *medRxiv are preprint servers: "[T]hese are preliminary reports that have not been peer-reviewed. They should not be regarded as conclusive, guide clinical practice/health-related behavior, or be reported in news media as established information."

medRxiv: Nasal-Swab Testing Misses Patients with Low SARS-CoV-2 Viral Loads (14 June 2020)

"The urgent need for large-scale diagnostic testing for SARS-CoV-2 has prompted pursuit of sample-collection methods of sufficient sensitivity to replace sampling of the nasopharynx (NP). Among these alternatives is collection of nasal-swab samples, which can be performed

by the patient, avoiding the need for healthcare personnel and personal protective equipment. Previous studies have reached opposing conclusions regarding whether nasal sampling is concordant or discordant with NP.

To resolve this disagreement, we compared nasal and NP specimens collected by healthcare workers in a cohort consisting of individuals clinically suspected of COVID-19 and outpatients known to be SARS-CoV-2 RT-PCR positive undergoing follow-up. We investigated three different transport conditions, including traditional viral transport media (VTM) and dry swabs, for each of two different nasal-swab collection protocols on a total of 308 study participants, and compared categorical results and Ct values to those from standard NP swabs collected at the same time from the same patients. All testing was performed by RT-PCR on the Abbott SARS-CoV-2 RealTime EUA (limit of detection [LoD], 100 copies viral genomic RNA/mL transport medium). We found high concordance (Cohen's kappa >0.8) only for patients with viral loads above 1,000 copies/mL. Those with viral loads below 1,000 copies/mL, the majority in our cohort, exhibited low concordance (Cohen's kappa = 0.49); most of these would have been missed by nasal testing alone.

Previous reports of high concordance may have resulted from use of assays with higher LoD (≥1,000 copies/mL). These findings counsel caution in use of nasal testing in healthcare settings and contact-tracing efforts, as opposed to screening of asymptomatic, low-prevalence, low-risk populations. Nasal testing is an adjunct, not a replacement, for NP."

medRxiv: Assessment of spread of SARS-CoV-2 by RT-PCR and concomitant serology in children in a region heavily affected by COVID-19 pandemic (14 June 2020)

" Several studies indicated that children seem to be less frequently infected with SARS-CoV-2 and potentially less contagious. To examine the spread of SARS-CoV-2 we combined both RT-PCR testing and serology in children in the most affected region in France, during the COVID-19 epidemic.

From April 14, 2020 to May 12, 2020, we conducted a cross-sectional prospective, multicenter study. Healthy controls and pauci-symptomatic children from birth to age 15 years were enrolled by 27 ambulatory pediatricians. A nasopharyngeal swab was taken for detection of SARS-CoV-2 by RT-PCR and a microsample of blood for micro-method serology.

Among the 605 children, 322 (53.2%) were asymptomatic and 283 (46.8%) symptomatic. RT-PCR testing and serology were positive for 11 (1.8%) and 65 (10.7%) of all children, respectively. Only 3 children were RT-PCR-positive without any antibody response have been detected. The frequency of positivity on RT-PCR for SARS-CoV-2 was significantly higher in children with positive serology than those with a negative one (12.3% vs 0.6%, p<0.001). Contact with a person with proven COVID-19 increased the odds of positivity on RT-PCR (OR 7.8, 95% confidence interval [1.5; 40.7]) and serology (15.1 [6.6; 34.6]).

In area heavily affected by COVID-19, after the peak of the first epidemic wave and during the lockdown, the rate of children with positive SARS-CoV-2 RT-PCR was very low (1.8%), but the rate of positive on serology was higher (10.7%). Most of PCR positive children had at the same time, positive serology suggesting a low risk of transmission."

Webinar

WHAT: How will a COVID-19 Vaccine be Delivered? International Vaccine Access Center

"When a COVID-19 vaccine becomes available, it will effectively stop disease transmission only if it reaches the people who need it. Many decisions go into developing a strategy for the delivery of a new vaccine, including planning for distribution challenges, communication around vaccine efficacy and safety, and planning for limitations in production capacity. Experts on epidemiology, policy, and advocacy at the International Vaccine Access Center will engage participants to consider decision-making processes and opportunities for innovation to optimize delivery and impact."

WHEN: Wednesday, 17 June 2020 1300-1400 ET

REGISTER: https://jh.zoom.us/webinar/register/WN_STVrSwb4TpiK_rGWnhDM_w

In Brief

The FDA has revoked the emergency use ruling for hydroxychloroquine to treat COVID-19 (FDA).

The CDC has (finally) released guidance on how people can minimize risk when going into public spaces (CDC) or planning events with groups (CDC); they also released testing recommendations (CDC).

Beijing has started widespread testing to beat back another eruption of coronavirus cases (WashPo).

A new airflow model could help reduce indoor exposure to aerosolized coronavirus (NIST).

Getting Back Out There

Passengers on an American Airlines flight from New York to Los Angeles in mid-March were exposed to COVID-19, but no one in public health told them they were exposed (LATimes).

Many states, including North Carolina, Florida, Texas, Arizona, California, and Hawaii, are seeing spikes in coronavirus cases (Reuters; see NYT for breakdown of data by state).

You may have to wait longer for everything, and in longer lines (Wired).

Librarians and tax assessors are stepping in to help with contact tracing (NPR).

"Public-health researchers use the infection fatality rate to gauge how to respond to a new disease, but it's tricky to calculate" (Nature).

Treatments and Vaccines

Regeneron will start multisite clinical trials to test its dual antibody cocktail, REGN-COV2, as both a prophylactic and treatment (Regeneron).

Sinovac Biotech announced preliminary data shows that CoronaVac, its COVID-19 vaccine, generated immune responses, suggesting it might protect against the coronavirus (STAT).

To deal with COVID-19, many mass vaccination efforts have been halted, with serious consequences (NYT).

Disparities

Instead of looking at obesity and diabetes for COVID-19 risks, we should be looking at social factors like race (STAT). [See working paper: http://ceepr.mit.edu/files/papers/2020-009.pdf]

Black churches are offering coronavirus testing in efforts to fix disparities (NPR).

COVID's Other Victims

Public health workers have quit, retired, or been fired due to backlash and overwork dealing with the pandemic (AP).

The latest 'victims' of the pandemic: prestigious medical journals (NYT). See report #19 for more on the state of COVID-19 literature (SharePoint).

With anti-vaccine and misinformation running rampant online, one public health group wants to teach pro-vaccine people to fight fire with fire (Wired).

Mental Health and Wellness

Mental health care systems are under a lot of strain, especially in hard-hit areas (KHN).

If you were one of the many people who bought up a lot of toilet paper for the pandemic, you were probably just looking for a symbol of safety and attempting to have a sense of control over uncertainty (Ars Technica). No, really: there's a study to back that up (PLOS One).

Long Reads

Here are some reasons why experts were wrong with they said US hospitals would be overwhelmed by COVID-19 patients (ProPublica).

Coronavirus experts warned that the next great pandemic would be a coronavirus, but research funding went to studying other threats (Undark).

"Amid the dual crises of a global pandemic and a reckoning with systemic racial injustice, health workers and health educators are grappling with a momentous question that hovers between personal and professional: how much of an activist should a health care worker be?" (STAT)

So You Survived COVID-19…

You could end up with a $1.1 million hospital bill (Time).

If you are thinking about going to Disney World, you still have to wait a bit (cnet).

Maybe just get a t-shirt [TM pending] and call it done (USAToday).

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In Brief

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